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DIABETESFORUM

Stockholm 21-22 mars 2013

Gastropares

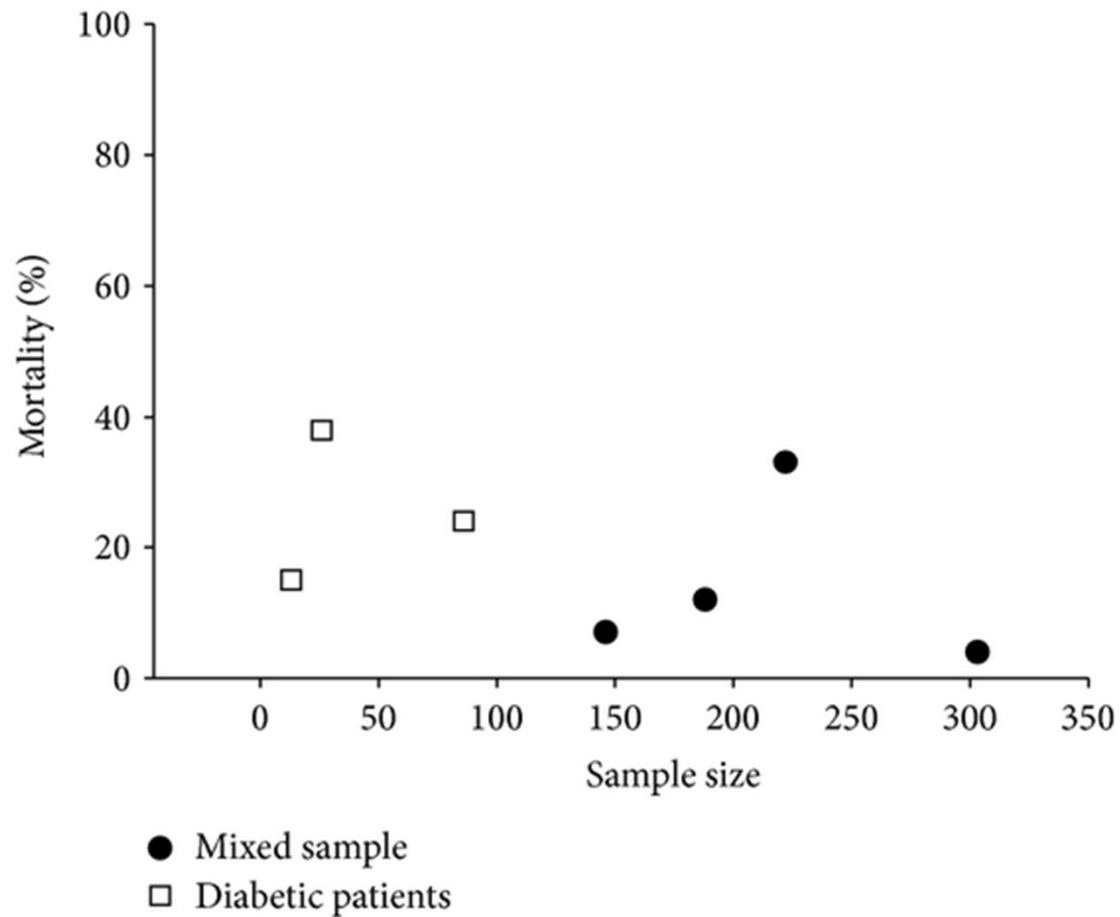
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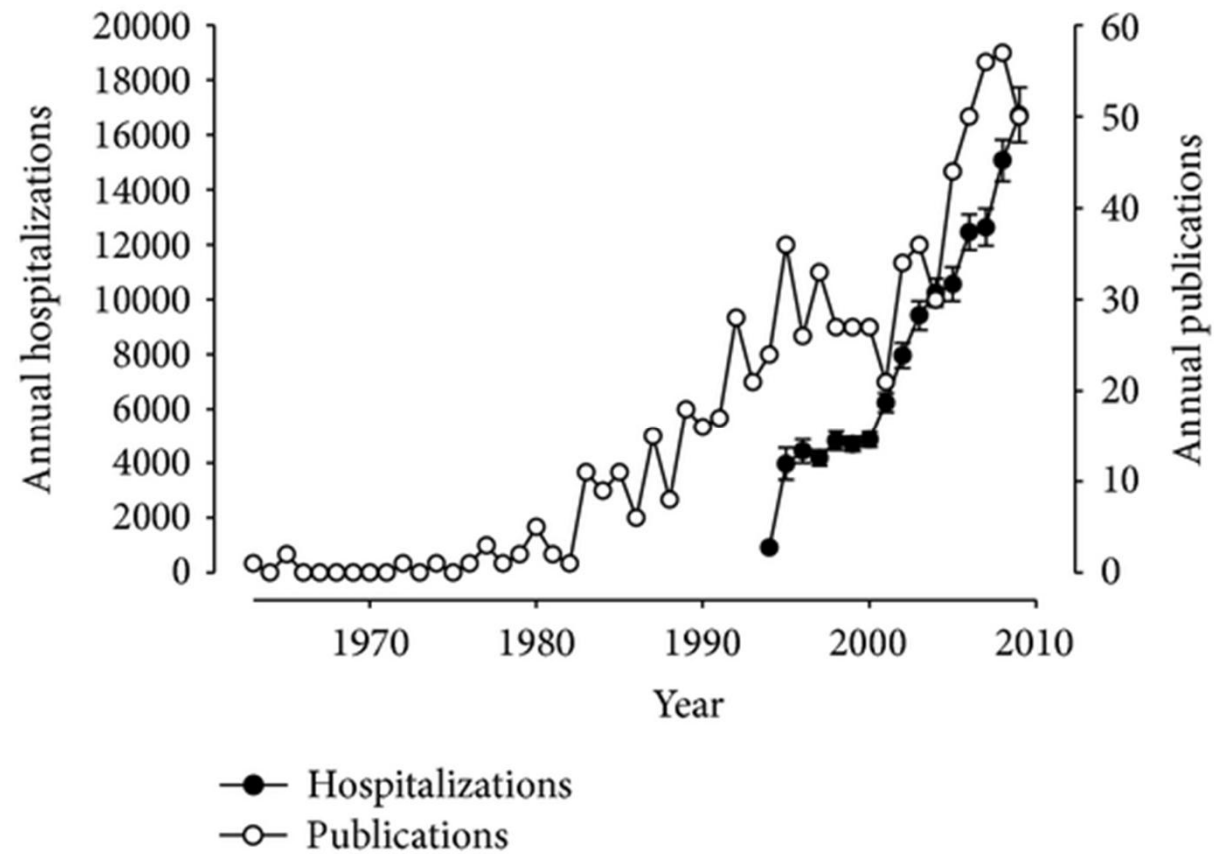
Gastroparesis är det viktigt?





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Gastropares Sjukvård och publikationer



Hasler 2011



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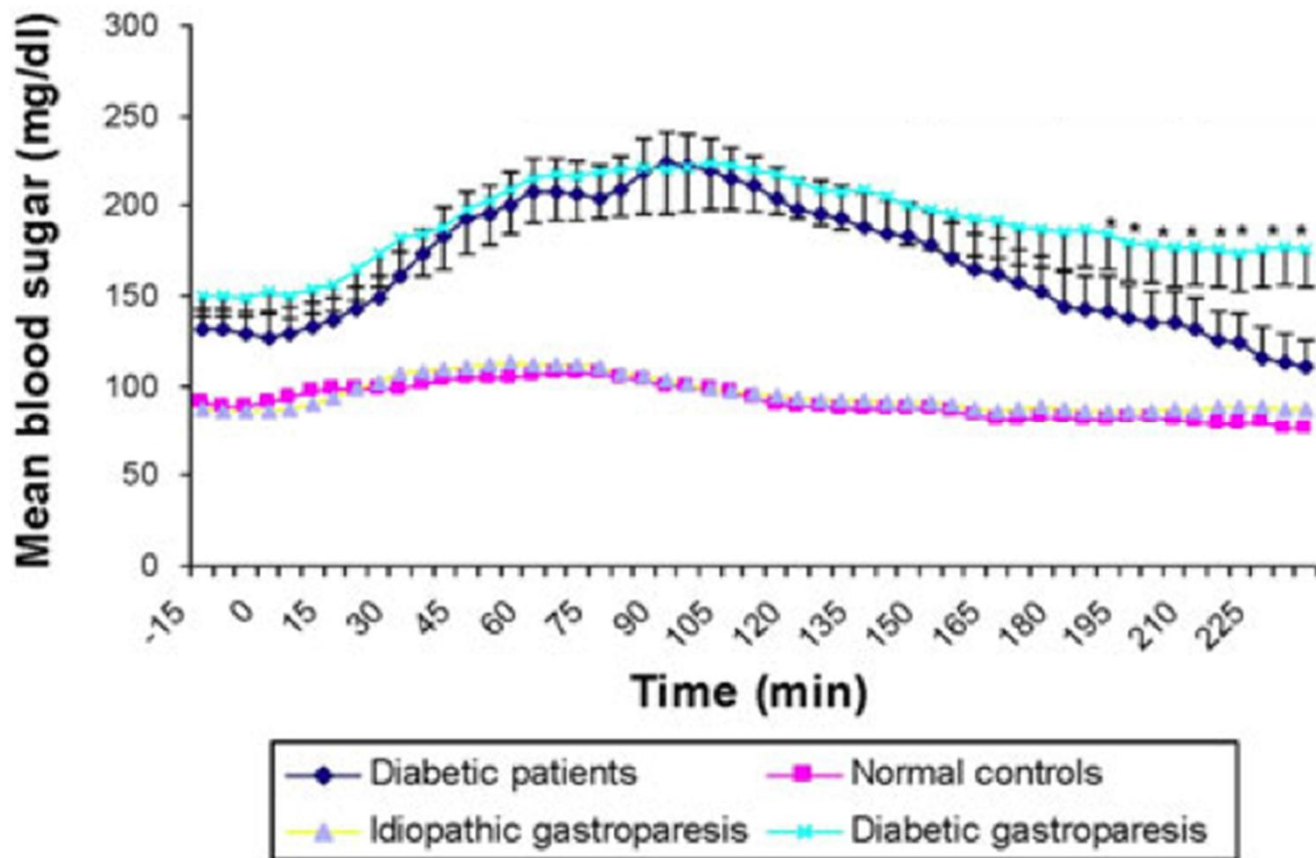
Problemet?

Ventrikeltömning \ddot{E} insulin - glukos

- ” Postprandiell hypoglykemi
- ” Postprandiell hyperglykemi



Postprandiell hyperglykemi





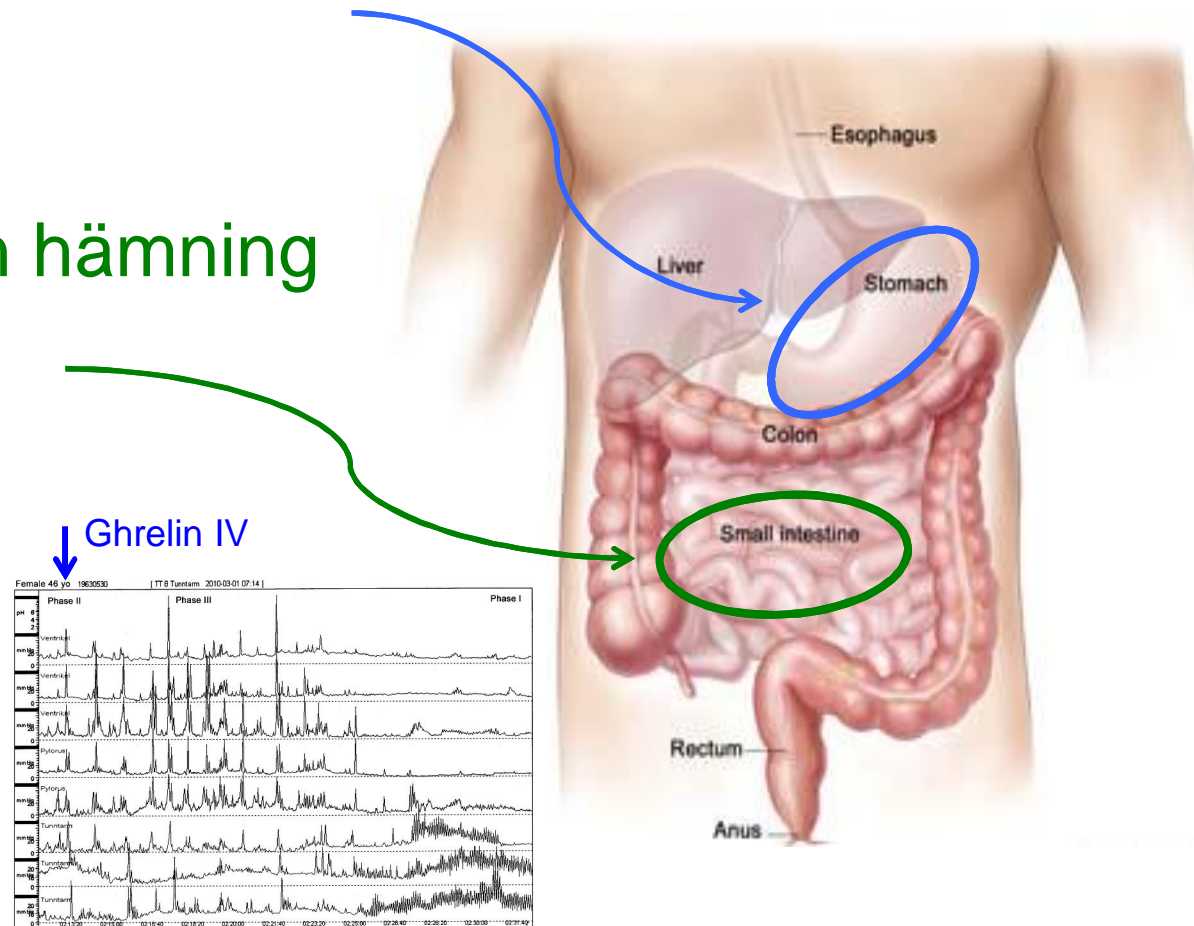
Två mekanismer !

” Minskad muskulär aktivitet

- . Ghrelin
- . Motilin

” Ökad inkretin hämning

- . GLP-1
- . Fett



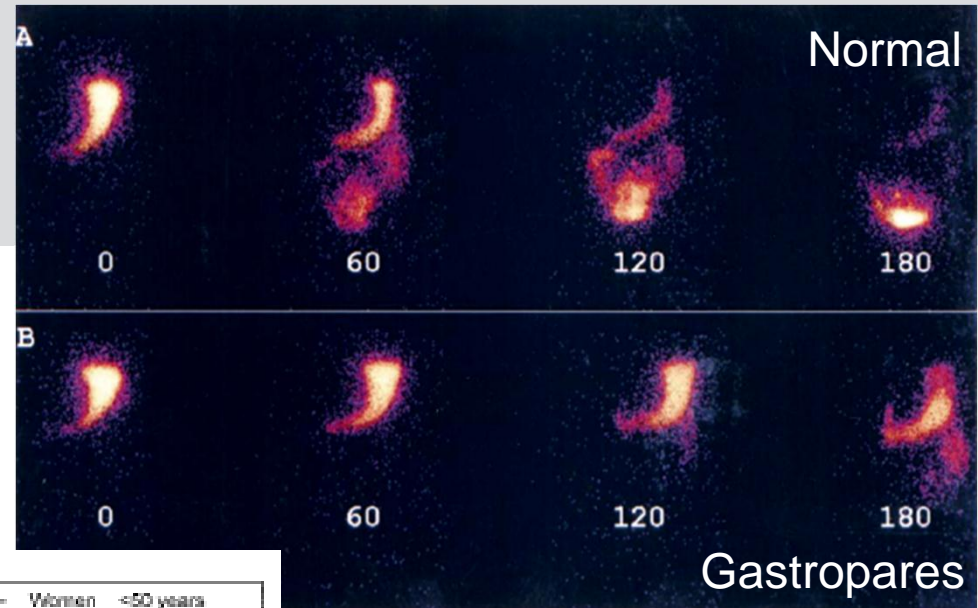
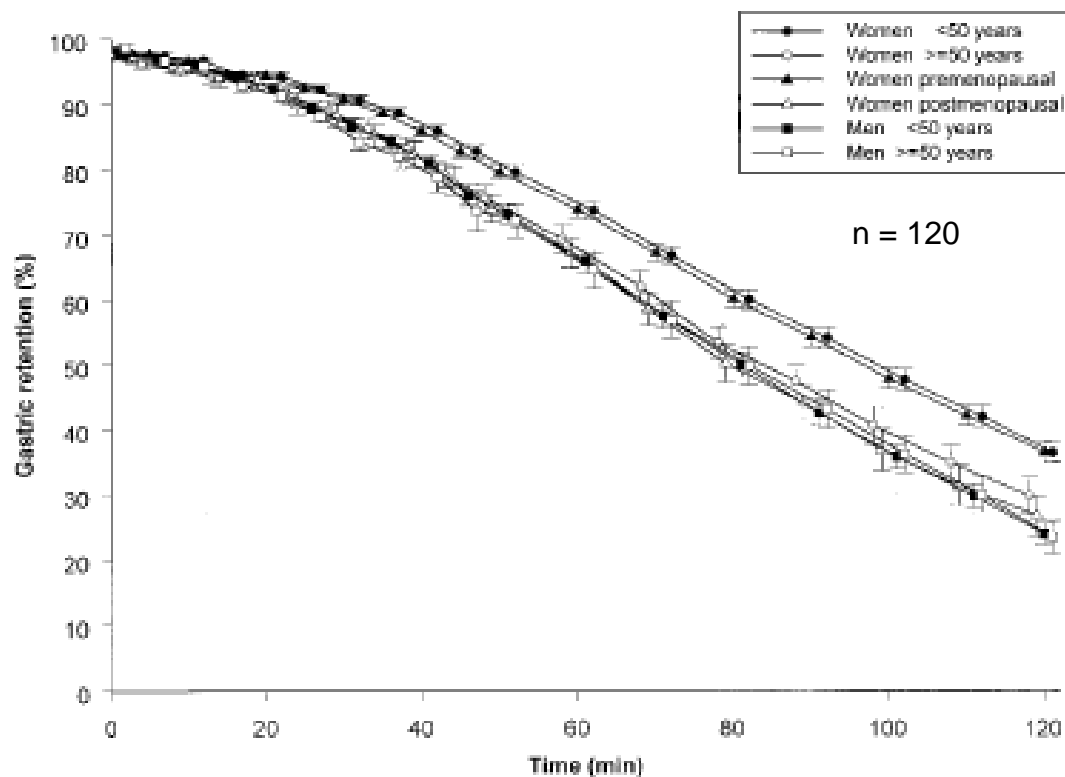
Migrerande
motorkomplexet
(MMC)



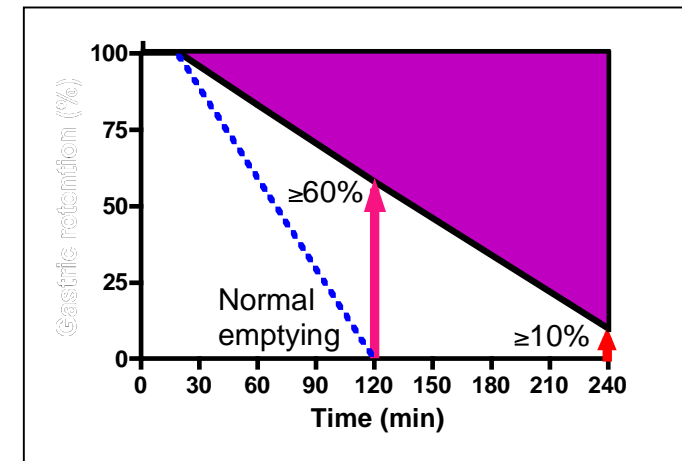
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Ventrikeln

Skintigrafisk Ventrikeltömning ^{99m}Tc



Definition



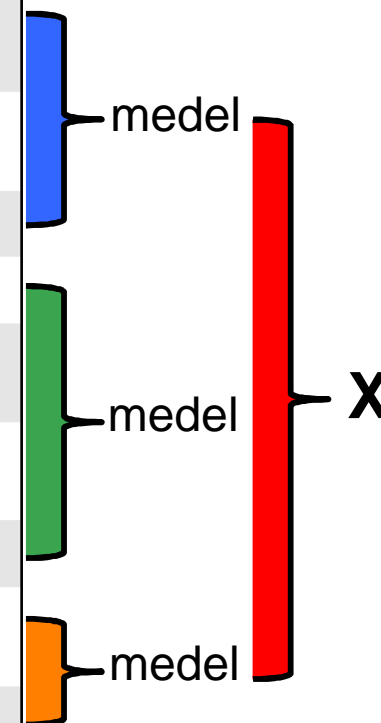


Ventrikeltömning utan skintigrafi . Gastroparesis Cardinal Symptom Index

GCSI

		Ej haft	Mycket mild	Mild	Måttlig	Svår	Mycket svår
1.	Illamående (kvaljningskänslor som om du skulle kräkas)	0	1	2	3	4	5
2.	Ulkningar (kvaljningar som om du skulle kräkas men inget kommer upp)	0	1	2	3	4	5
3.	Kräkningar	0	1	2	3	4	5
4.	Mättnadskänsla	0	1	2	3	4	5
5.	Oförmåga att äta upp ett normalt mål mat	0	1	2	3	4	5
6.	En känsla av att vara övermätt efter måltider	0	1	2	3	4	5
7.	Brist på aptit	0	1	2	3	4	5
8.	En känsla av uppkördhet (att du behövde lossa på dina kläder)	0	1	2	3	4	5
9.	Magen eller buken är synbart större	0	1	2	3	4	5

Matematik

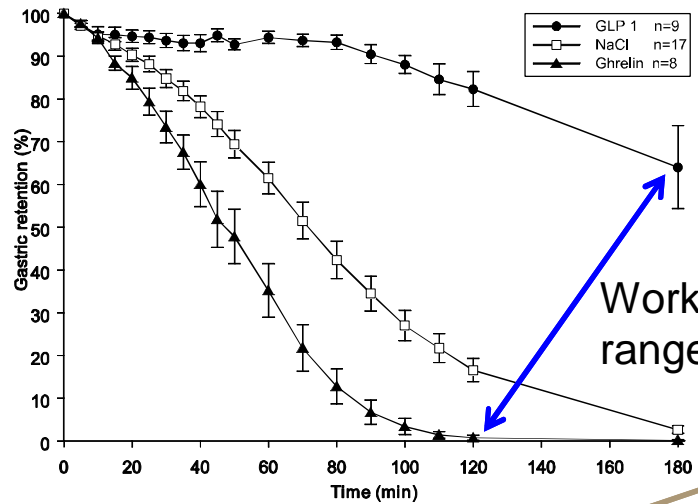


Cut-off för gastropares = 2,66; sens 58%, spec 56%



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Mag-tarmkanalen & endokrinologi



↑ Insulin

↑ Insulin

GIP

GLP-1

Motilin

Ghrelin

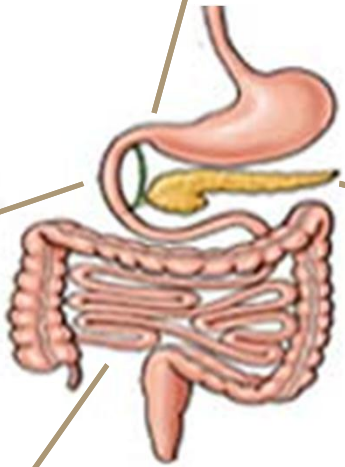
↕ Insulin

Insulin
Glukagon

↓ Insulin

Leptin

Fettväv





Vad har vi idag?

“ Metoklopramid (Primperan)

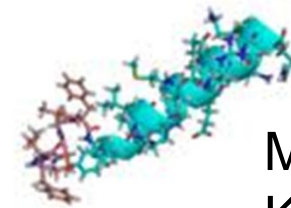
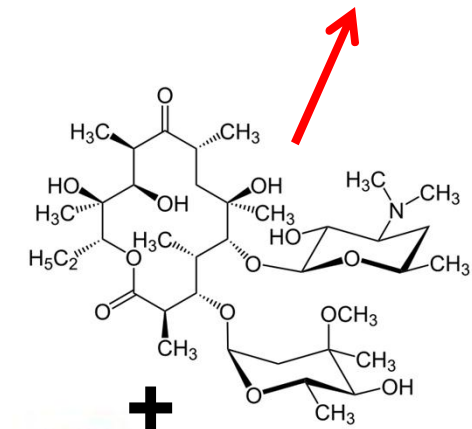
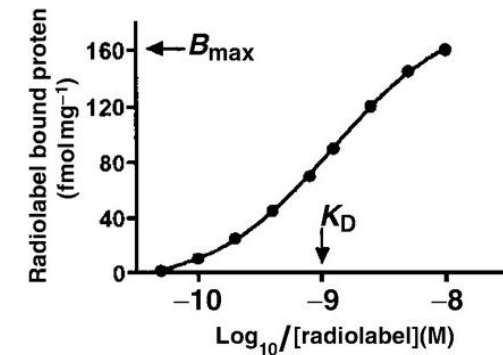
- . D₂ receptorantagonist
- . 5HT₃ receptoragonist

“ Domperidon (Motilium; ej rab)

- . D₂ receptorantagonist

“ Erytromycin (Ery-Max, Abbotcin)

- . Motilinreceptoragonist
- . 14 C-atomer i ringen
- . 1-3 mg/kg/måltid

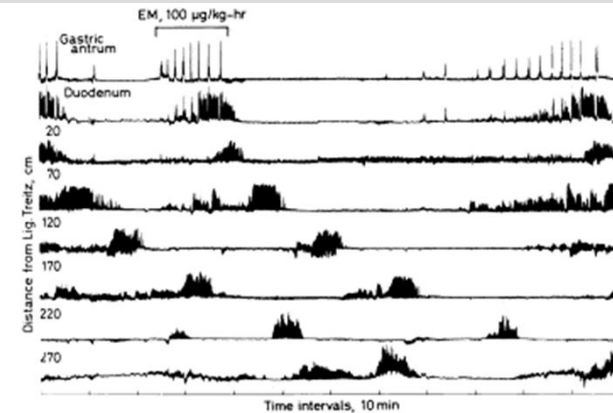


Motilinreceptor
 $K_d = 1.2 \text{ nM}$



Fungerar det?

Erytromycin
stimulerar
MMC



Kliniska prövningar med erytromycin

Study (Reference)	n	Group	Design	Dose	T _{1/2} Decrease	Sxs	Individual Sx Scores Given	Jadad Score
Erbas <i>et al.</i> 1993(14)	13	D	OL, XO (R vs E) 3 wk Tx	250 mg <i>t.i.d.</i> (E) 10 mg <i>t.i.d.</i> (R)	50% (E) 44% (R)	11/13 impr (E) 7/11 impr (R)	Yes	1
Richards <i>et al.</i> 1993(15)	10	D & I	OL 4 wk Tx	500 mg <i>p.o.</i> (ac & qHS)	44% (2 h retention)	2/14 impr (ITT analysis)	Yes	1
Ramirez <i>et al.</i> 1994(13)	9	V & A	OL 2 wk	150 mg <i>p.o. t.i.d.</i>	40%	3/9 impr	No	0
Fiorucci <i>et al.</i> 1994(12)	12	PSS	OL 4 wk	250 mg <i>p.o. t.i.d.</i>	60%	10/12 impr	No	0
Samsom <i>et al.</i> 1997(16)	12	D	DB, PC, XO 2 wk Tx	250 mg <i>p.o. t.i.d.</i>	Not Done	ns	No	2

D = diabetes; DB = double blind; E = erythromycin; I = idiopathic; Impr = improved; ITT = intention to treat; OL = open label; NS = not significant; PC = placebo controlled; PSS = progressive systemic sclerosis; R = reglan; Sx = symptom; Tx = treatment duration; V & A = vagotomy and antrectomy; XO = crossover.

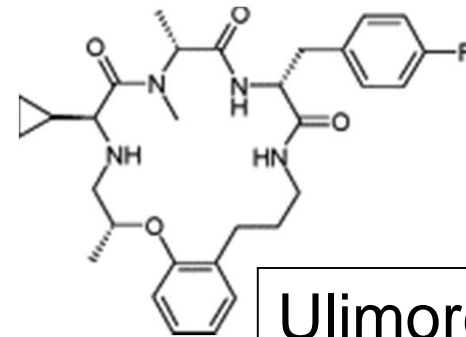


Nya GastroProkinetika

” Ghrelin-analoger

- . TZIP-101 (IV, ulimorelin)
- . TZIP-102 (PO, ipamorelin)

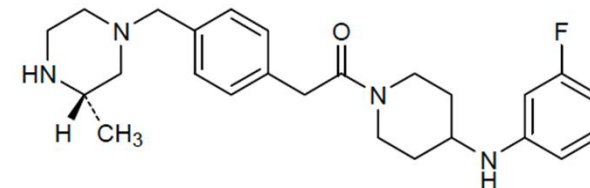
Fas 2a, fas 2b



Ulimorelin

” Motilin-analog

- . GSK962040 (PO, camicinal)
- . Fas 2

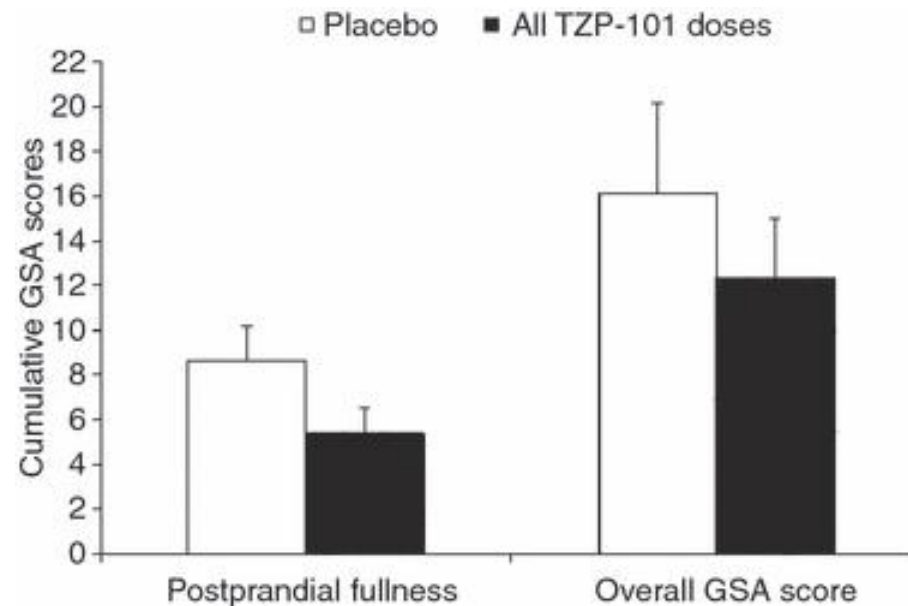
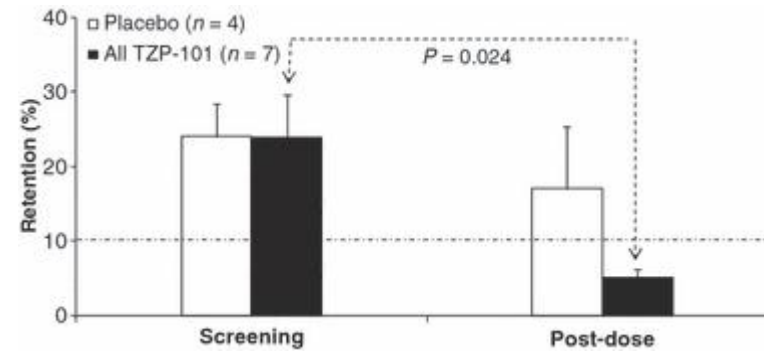
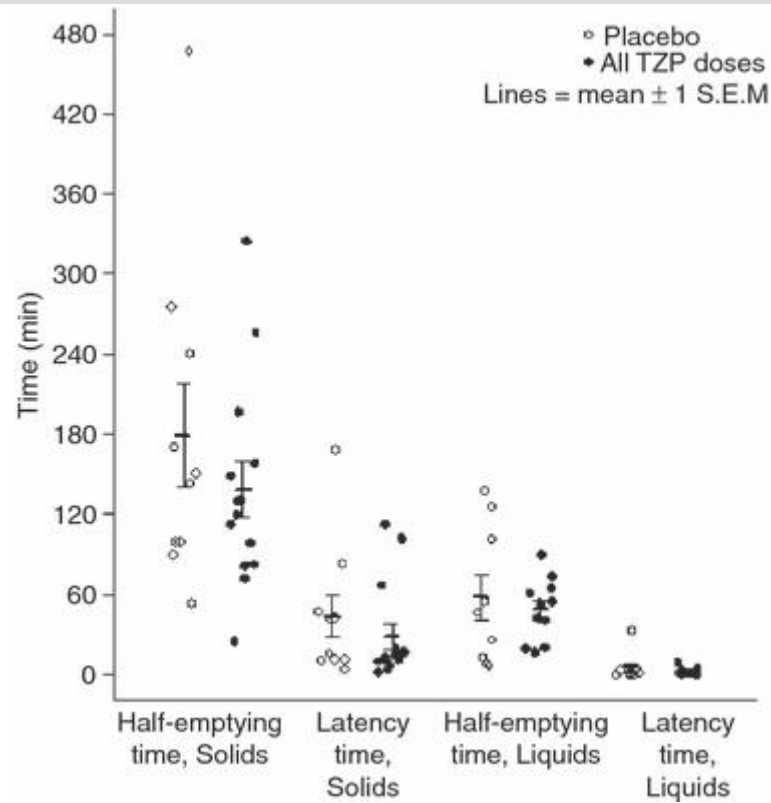


Camicinal



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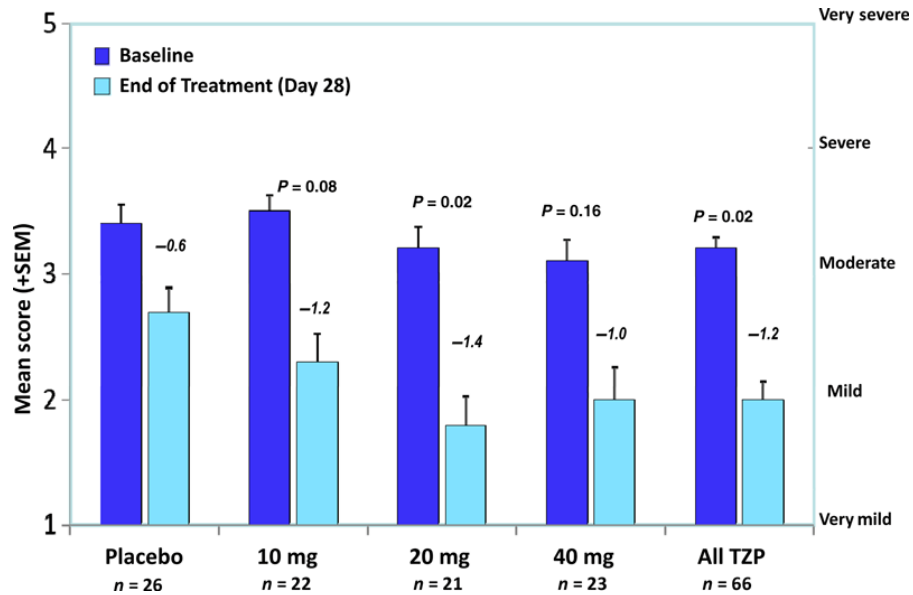
Ulimorelin



Ejskjaer et al 2009



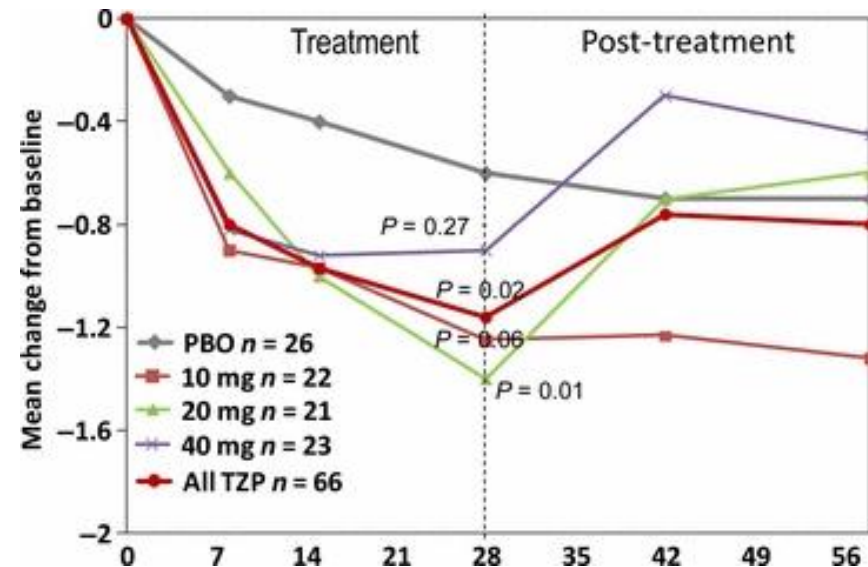
Ipamorelin



Effektparametrar

“Förbättring av symtom

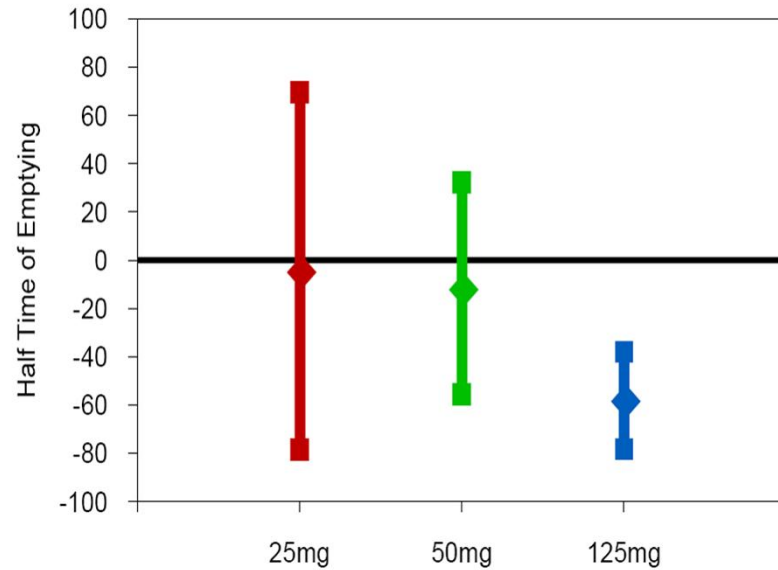
“Påskyndad ventrikeltömning





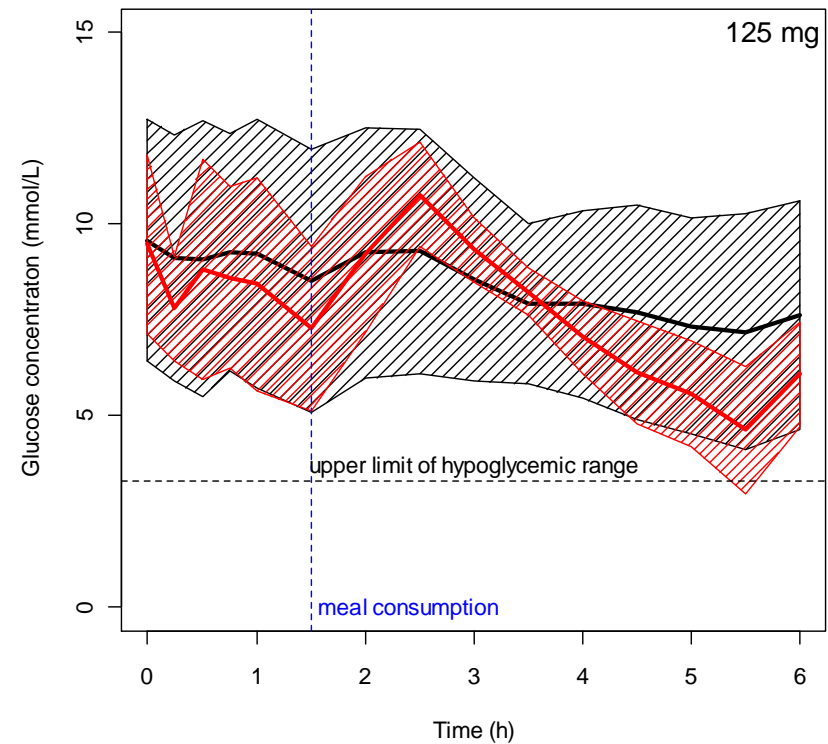
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Camicalinal



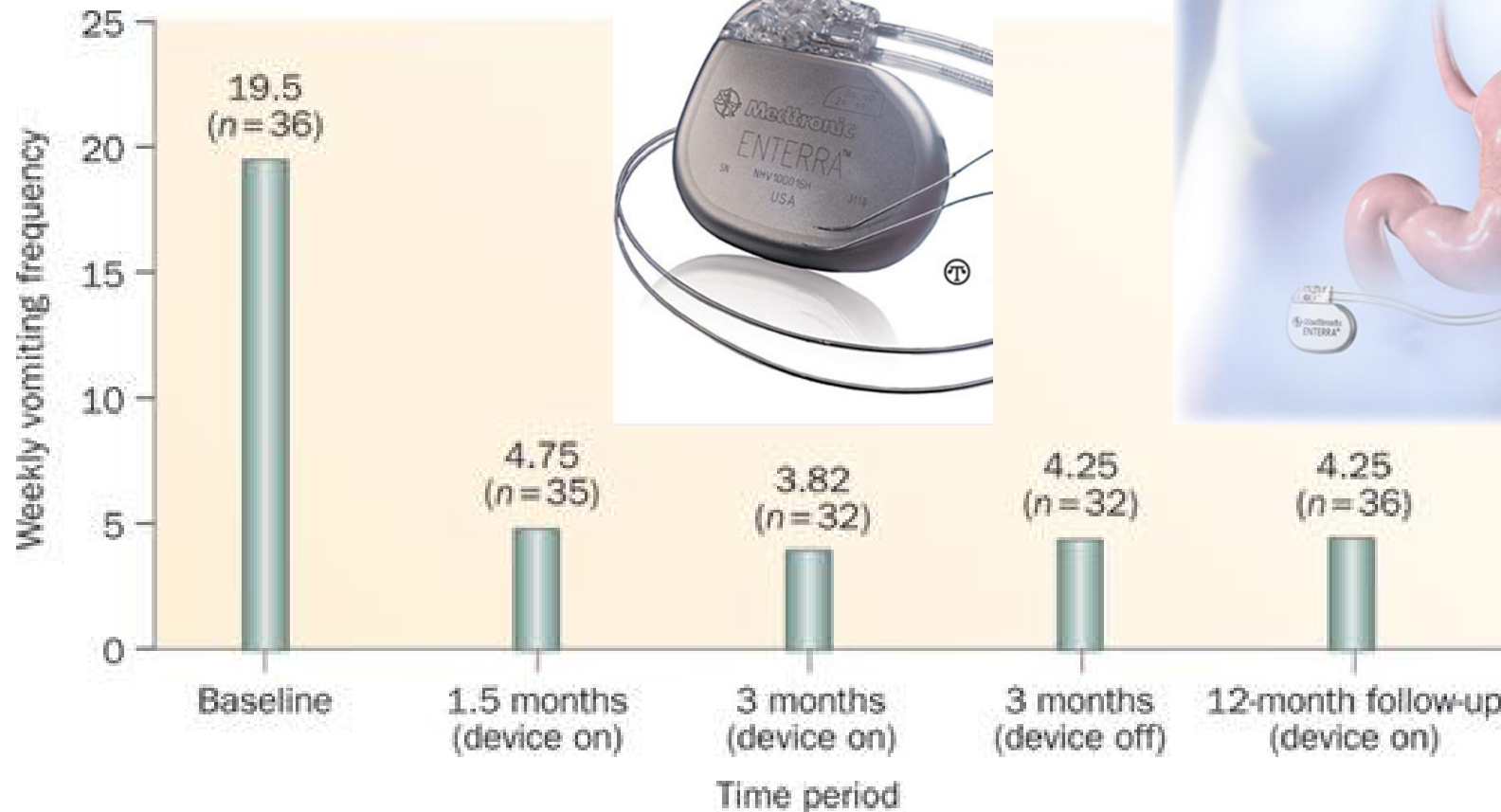
Effektparametrar

“Stimulerad ventrikeltömning
“Rektifierat P-Glukos





Till sist - Gastric pacingÅ .



• vid kräkningar



Slutord

Dags för paradigmskifte?

